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A Mathematical Model for the Effect of Domestic Animals on Human African Trypanosomiasis (Sleeping Sickness)

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Cover Page Footnote

Special thanks to Dorothy Wallace and her students, for sharing their earlier work and drawing our attention to mathematical models of trypanosomiasis.

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ABSTRACT

Human African Trypanosomiasis (HAT) is a parasite infection that is spread by the bites of tsetse flies, and it is almost 100% fatal if left untreated (World Health Organization, "Neglected"). Our hypothesis is that by adding domestic animals to areas where humans are found (villages and plantations), we can reduce the amount of biting on humans, and therefore reduce the rate at which humans become infected. Numerical simulations supported our hypothesis, showing that increasing the number of domestic animals (pigs in our model) slows down the spread of the disease in both humans and domestic animals.

Keywords: epidemiology, mathematical biology, human African trypanosomiasis

Introduction

The World Health Organization classifies HAT as a neglected tropical disease even though an estimated 65 million people are at risk (World Health Organization, "Trypanosomiasis"). HAT is a disease that is a major problem in rural Africa, where the tsetse flies that transmit the trypanosome parasite thrive. The HAT parasite comes in two forms: one, the gambiense HAT, is endemic in west and central Africa and causes over 95% of cases. The second, the rhodesiense HAT, is endemic in east and southern Africa and accounts for the remainder of cases. Once the parasite reaches the brain it causes a progressive neurological breakdown. Some of the symptoms are: fever, abnormal behavior, changes to sleep–wake patterns, coma, and eventually death if the patients are not treated. There are several treatments available against the parasite; however, the current drugs are either complex to administer, expensive and require hospitalization, or toxic and might kill the patient (World Health Organization, "Control").

Over the years several control solutions were formulated such as insecticides, placing traps, using sterile vectors, eliminating animal reservoirs, and more. However, they are expensive and not optimal in the long run because they require ongoing maintenance. So, while reducing the transmission of the parasite may seem like the optimal solution for the spread of the disease, we believe that a different approach is necessary. It is known that animals (especially domestic animals) play a key role as a reservoir in the transmission of the parasite. Therefore, an approach of removing domestic animals has been considered (Maudlin 688). However, this approach forces the fly to look for other sources of food, such as humans.

Moreover, previous work has treated female and male flies the same, but one study found that in villages where domestic pigs are

found, the female fly is much more aggressive towards pigs than humans (Chalvet-Monfray 208). Another study found that male and female flies have significantly different lifespans, and the Trypanosome parasite takes about 3 weeks to develop in the fly's body before it can be transmitted by the fly (Centers for Disease Control and Prevention). We also found literature that indicates that female flies have a stronger preference for domestic animals over humans (Gouteux 100). These simple but important details shaped our hypothesis that by adding domestic animals to areas where humans are found (villages and plantations), we can reduce the amount of biting on humans, and therefore reduce the rate at which humans become infected. The aim of our work is to create a differential equations epidemiology model for the spread of the vector-borne disease, to test whether our hypothesis can be used to reduce the impact of the disease.

Model

Our research is based on several important factors. Firstly, the parasite. The first blood meal is very important as this food is used to develop the flight muscles in the thorax, which are undeveloped at birth. Flies will most likely get infected by T. brucei in this weak state if they feed on an infected host, but the chance of getting infected by the parasite afterwards are extremely low (Wijers 319-320). When an uninfected fly bites an infected host, the parasites transform into procyclic trypomastigotes in the fly's midgut, multiply by binary fission, leave the midgut, and transform into epimastigotes. The epimastigotes reach the fly's salivary glands and continue multiplication by binary fission. The cycle in the fly's body takes approximately three weeks (Centers for Disease Control and Prevention). That means that in these three weeks the fly cannot infect other hosts. Yet, literature does not consider whether the male fly is capable of transmitting the disease. We first hypothesized that because male flies live only up to three weeks (Pollock 22), they should be unable to transmit the disease and therefore are irrelevant for its spread in humans. Secondly, we considered the preference of female flies for pigs. One study stated that in villages where domestic pigs are found, as few as 1% of the bites from the tsetse flies were on humans, while in the plantations where there are no domestic animals and only wild animals, the average was between 20%-30% of fly bites on humans (Chalvet-Monfray 208). Such villages in the Ivory Coast, where HAT is endemic, include a typical population of 300 humans, 50 domestic animals, and 5000 flies. Other research stated that male flies are more aggressive to humans than female flies (Gouteux 100). Another factor to consider is that in the villages, fly aggressiveness is low and they prefer to feed on pigs rather than on people (Gouteux 100). Given the above factors we created a set of equations to model our hypothesis.

<u>The model includes the following equations:</u>

The rate of change in the susceptible human population is given by the rate of birth less the rate at which susceptible humans become infected and the death rate.

$$s_h' = \mu_h - ab_h(1-\varphi)m_h f_i /F * s_h/N_h - \mu_h s_h/N_h$$

The rate of change in the infected human population is given by the rate at which susceptible humans become infected less the rate at which infected humans are removed from the infected population (hospitalized) and the death rate.

$$i_h' = ab_h m_h (1-\varphi)\, s_h/N_h\, f_i /F - \rho i_h/N_h - \mu_h i_h/N_h$$

The rate of change in the removed human population is given by the rate at which humans are removed from the infected population less the death rate.

$$r_h' = \rho i_h - \mu_h r_h$$

The rate of change in the susceptible pig population is given by the rate of birth less the rate at which susceptible pigs are infected and the death rate.

$$s_p' = \mu_p - ab_p m_p \varphi s_p/N_p \, f_i/F - \mu_p s_p/N_p$$

The rate of change in the infected pig population is given by the rate at which susceptible pigs are infected less the death rate.

$$i_p' = ab_p m_p \varphi \, s_p/N_p \, f_i/F - \mu_p i_p/N_p$$

The rate of change in the female fly population is given by the rate of female flies' deposition times the rate at which it becomes infected from an infected host less the death rate.

$$f_i' = (F/2\ell) \, \sigma \, a \, b_v \{[m_h(1-\varphi) \, i_h/N_h + m_p \varphi i_p/N_p]\} - \mu_f f_i/F$$

Figure 1. ***Transmission Dynamics***

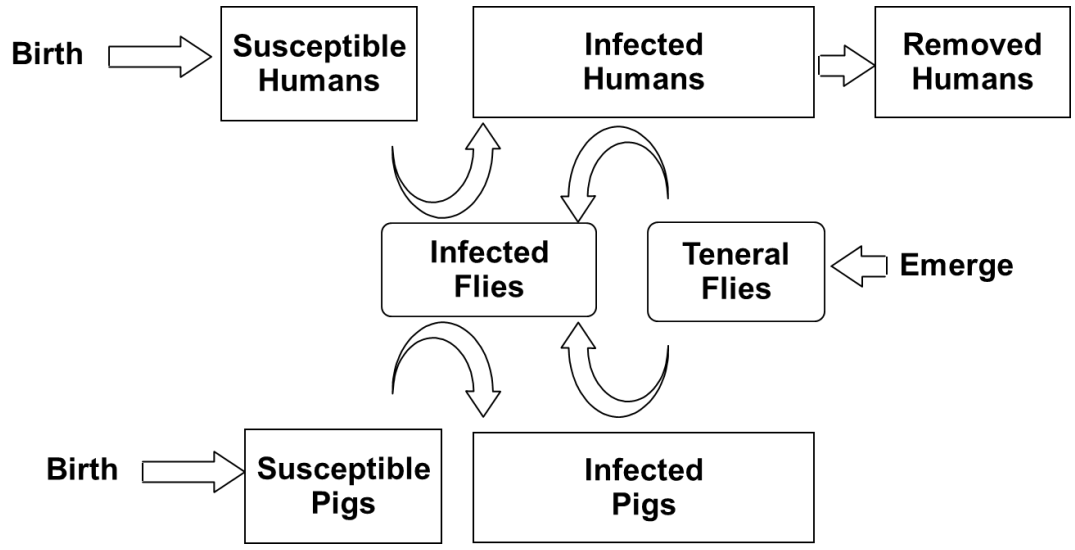


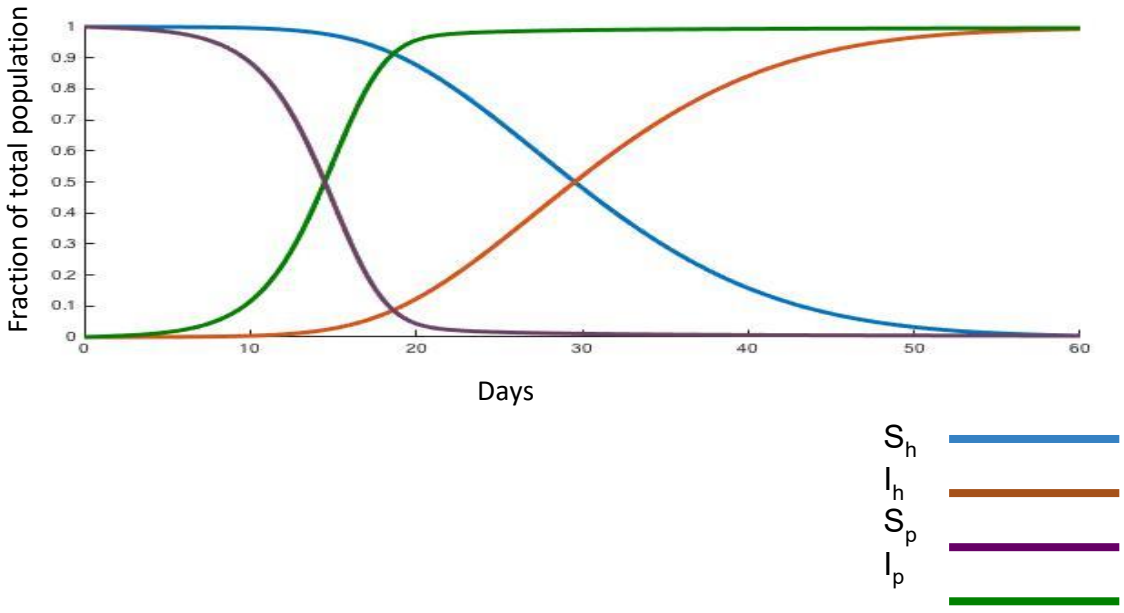
Table 1. ***Values of all variables and constants***

Parameter	Value	Meaning	Source
σ	**0.66**	percent of fly eggs that survive to become adult females	Estimation
a	**0.3**	biting rate of flies for first meal, same for all hosts	Rogers et al., 1994
μh	**0.00007**	birth/death rate of humans (40 years)	Estimation
μp	**0.003**	birth/death rate of domestic animals (pigs)	Estimation
μf	**0.01**	death rate of female flies	Madsen et al., 2013
bh	**0.62**	percent bites on humans resulting in infected humans	Rogers, 1988
bp	**0.62**	percent bites on pigs resulting in infected pig	Rogers, 1988
bv	**1**	percent of flies infected when biting infectious host	Rogers et al., 1994
l	**9**	fly egg production rate (1 per 9 days)	Pollock, 1982
ϕ	**0.97**	preference of flies for pigs	Chalvet-Monfray et al., 1998
ρ	**0.1**	Removal rate of sick humans from infectious population	Estimation
Nh	**300**	Total number of humans	Gouteux and Laveissiere, 1982
Np	**100**	Total number of domestic animals (pigs)	Gouteux and Laveissiere, 1982
F	**1000**	Total number of female flies	Estimation
Mp	**F/Np**	ratio of female flies to host (pigs/domestic animals)	Calculation
Mh	**F/Nh**	ratio of female flies to host (humans)	Calculation

Results

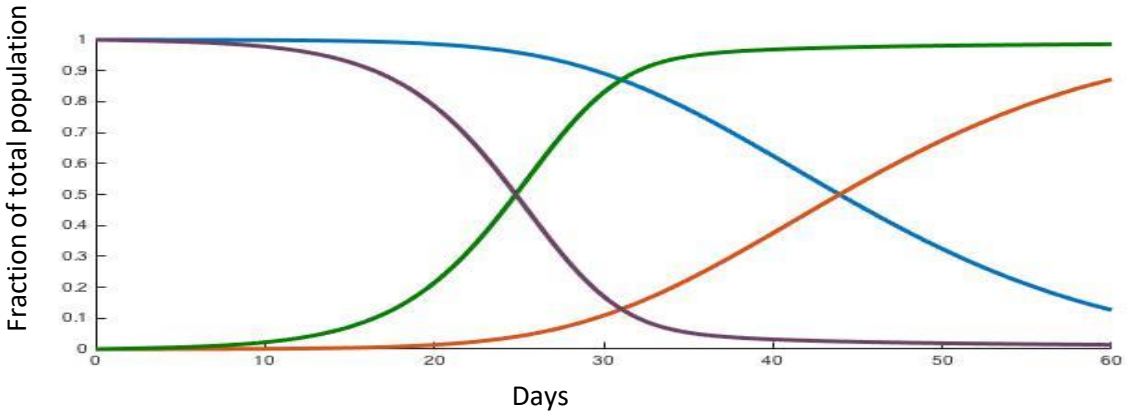
The equations were solved numerically using Euler's method on Matlab as shown in Figures 2 and 3. Initially, we started with 300 susceptible humans, 100 susceptible pigs, and 1000 female flies (5 of which were infected). In Figure 2 the population of the susceptible pigs is cut in half after about 14 days, as the population of the infected pigs increases at the same rate. Also, we can see that the population of the susceptible humans is cut in half after about 30 days, as the population of infected humans increases. We can see that the pigs become infected more quickly than the humans, since the female fly has a much higher preference towards pigs. It is also clear that given enough time all of the hosts will become infected.

Figure 2. ***Equal numbers of humans and pigs***



In Figure 3 we increased the number of pigs to 200 and kept the other values the same. This figure shows that the population of the susceptible pigs is now reduced by half after about 25 days, as the population of the infected pigs increases at the same rate. Also, we can see that the population of the susceptible humans is cut in half after about 44 days, as the population of infected humans increases. We can see that the pigs are getting infected quicker as expected again. It is also clear that given enough time all of the hosts will become infected.

Figure 3. ***Increase number of pigs***



Discussion

By looking at Figures 2 and 3, one can see that the hypothesis was supported—that increasing the number of pigs will slow down the disease. Also, by adding pigs rather than reducing their number we can alleviate stressors on villagers, as they are using the animals for work and as a food source. This result also shows how important several parameters are on this disease's containment, in particular, the preference parameter. As the literature indicated, female flies have about a 97% preference for pigs over humans, and so a small change in the number of pigs can cause a great change in the dynamic of the disease. We believe that the reason for the reduced speed of the disease's spread is that the flies prefer to feed on pigs and by increasing the pig population, the number of bites humans receive becomes minimal.

Conclusions and Future Directions

This work has shown that increases in the population of domestic animals (pigs) can have a positive effect on the spread of the disease in humans. Future research should focus on investigating the disease's parameter relationships which could also benefit village economics while reducing the impact of the disease. Furthermore, the possibility of developing a vaccine for the pigs would be a potentially beneficial direction to be modeled.

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